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c) identifying compounds where there is not an additive effect on metabolic rate as compounds which modulate the AMP-sensitive regulatory site.

A2

8. A method according to claim 7, which further comprises the steps of:

- contacting the compounds identified in claim 7 with mitochondria in the presence of a substrate for respiration in the presence of a buffer system and in the presence of AMP and measuring membrane potential,
- comparing the membrane potential in (a) with claim 7 step (b); and
- identifying compounds where there is not an additive effect on membrane potential as compounds which modulate the AMP-sensitive regulatory site.

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12. A method according to claim 11, which further comprises the steps of:

- contacting the compounds identified in claim 11 with mitochondria in the presence of a substrate for respiration in the presence of a buffer system and in the presence of AMP, measuring an index of metabolic rate and measuring the membrane potential;
- comparing metabolic rate and the membrane potential in (a) with claim 11 step (b); and
- identifying compounds where there is not an additive effect on metabolic rate and membrane potential as compounds which modulate the AMP-sensitive regulatory site.

15. A method according to any one of claims 3, 4, 11 and 12 wherein the index of metabolic rate is oxygen consumption.

A4

16. A method according to any one of claims 3, 4, 7, 11 and 12 wherein the mitochondria are isolated mitochondria or a suitable part or derivative thereof.

17. A method according to any one of claims 3, 4, 7, 11 and 12 wherein the mitochondria are skeletal muscle mitochondria or a suitable part or derivative thereof.

A5
19. A method according to any one of claims 3, 4, 7, 11 and 12 wherein the mitochondria are present in intact eukaryotic cells.

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21. A method according to any one of claims 3, 4, 7, 11 and 12 wherein a complex 1 inhibitor is present.

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22. A method according to any one of claims 3, 4, 7, 11 and 12 wherein the substrate is a succinate salt.

A7
24. A method according to any one of claims 3, 4, 7, 11 and 12 wherein the screening method is carried out in the presence of varying concentrations of an electron transport inhibitor.

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28. A screening method according to any one of claims 8 and 11, wherein the membrane potential is measured using ion selective electrodes.

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29. A screening method according to any one of claims 8 and 11 wherein the membrane potential is measured using fluorescent membrane potential dyes.

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30. A screening method according to claims 3, 7, and 11 wherein an inhibitor of ATP synthesis is present.

31. A method according to any one of claims 3, 7 and 11 for the identification of compounds which are suitable for use in the treatment of a body weight disorder.

32. A method according to any one of claims 3, 7 and 11 for the identification of compounds which are suitable for use in the treatment of obesity and related conditions.

A8
33. A method according to any one of claims 3, 7 and 11 for the identification of compounds which are suitable for use in the treatment of cachexia and related conditions.

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40. An assay method according to any one of claims 37 and 38 in which the labelled ligand is radiolabelled or fluorescently labelled atractylate or fluorescently labelled ATP or ADP.

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44. A screening method for identifying compounds which modulate the proton leak mediated by an ANC comprising the steps of:

- a) incubating a test compound with cells in which an ANC is upregulated and measuring an index of metabolic rate or membrane potential;
- b) incubating a test compound with control cells in which the ANC used in step a) is absent or is present at lower levels than in step a) and measuring an index of metabolic rate or membrane potential; and
- c) identifying a compound which gives rise to a different metabolic rate or different membrane potential in step a) compared to step b) as a compound which modulates the proton leak mediated by an ANC.

A11
50. A method or assay according to any one of claims 3, 7, 11, 34, 35, 36, 37, 41, 42, 43, and 44 further comprising the step of screening a compound identified as being suitable for use in the treatment of a body weight disorder in a further screen for suitability in treating a body weight disorder.

51. A method or assay according to any one of claims 3, 7, 11, 34, 35, 36, 37, 41, 42, 43, and 44 further comprising the step of screening a compound identified in a further screen for suitability in treating obesity or a related condition.

52. A method or assay according to any one of claims 3, 7, 11, 36, 43, 46 and 49 further comprising the step of screening a compound identified in a further screen for suitability in treating cachexia or a related condition.

53. A compound identifiable in a screening method or assay according to any one of claims 3 7, 11, 34, 35, 36, 37, 41, 42, 43, and 44.

54. A compound identified in a screening method or assay according to any one of claims 3, 7, 11, 34, 35, 36, 37, 41, 42, 43, and 44.

55. A compound according to claim 53 for use in medicine.

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56. A method for treating a body weight disorder in a patient the method comprising administering to the patient a compound according to claim 53.

57. Use of a compound according to claim 53 in the manufacture of a medicament for treating a body weight disorder.

Conclusion

All claims presently in the application are believed to be allowable over the art of record and early notice to that effect is respectfully solicited. Please charge any additional fee required for the timely consideration of this application to Deposit Account No. 19-4972.

Respectfully submitted,



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